Foreword

Nanomedicine

Twenty-five years of nano-bio-materials: have we revolutionized healthcare?

"Nanomedicine may not have completely revolutionized healthcare as yet, but it is on the way."

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The term 'nano' was coined back in 1990's to denote anything novel, progressive and futuristic. In sciences, the term 'nano' is a unit prefix that indicates one billionth (10^{-9}), a dimension, for example, that is larger than 'pico' (10^{-12}) and smaller than 'micro' (10^{-6}). In 1990s and up to middle 2000s, a material was considered as 'nano scale' at dimensions smaller than 1 μm. Nowadays, as the science and technology has progressed, in the physical sciences space, the term 'nano' refers to materials with dimensionality smaller than 100 nm, while in the biomedicine field 'nano' is used to describe any object with dimensions between 250 and 750 nm.

Nano-biomaterials, nano-medicine and nano-bio-interface are terms used interchangeably to denote tools, technologies and discoveries of nanotechnology that are utilized in medicine. The supremacy of nano-devices in medicine is founded on the fact that this scale closely imitates the small dimensionality of native cells and extracellular matric component and operates on the same small scale as several functions in the body. Thus, when we started developing nano-bio-materials, almost 25 years ago, we hypothesized that nano-scale devices would be more physiologically relevant than their macro-scale counterparts. Our aspiration was that these small devices would revolutionize healthcare with their massive impact. Where are we now?

The global nanomedicine market was valued at US$248 billion in 2014 and is projected to grow at a compound annual growth rate of 16.3% until 2019, reaching value of US$ 528 billion [1]. This is not surprising given that in Europe alone over €650 million were invested in nano-bio-related projects during the FP7 round of calls [EC, Personal Communication]. This staggering funding has resulted in exponential growth in the number of peer-reviewed publications (Figure 1). Proportional is the situation in commercial and clinical space as evidenced by 1756 patents (source: European Patent Office; Term Searched: 'nano' in title and 'medicine' in Title or Abstract) and over 116 currently registered clinical trials (source: clinicaltrials.gov; Term searched: 'nano'). The obvious question is what has really been achieved with all of this funding?

Advances in engineering have made available numerous top-down (e.g., imprinting lithography) and bottom-up (e.g., electrospinning) nano-fabrication technologies that are at the forefront of scientific and technological research and innovation for the development of two- and three- dimensional biomimetic structures. Two-dimensional imprinted devices have been used extensively to maintain phenotype fidelity of permanently differentiated cells or to precisely control stem cell lineage commitment during *in vitro* expansion [2–4]. The potential of three-dimensional electro-spun nanofibrous scaffolds as drug delivery vehicles and as means to direct neotissue formation has been well established [5–7]. Nanocarriers are being developed for sus-

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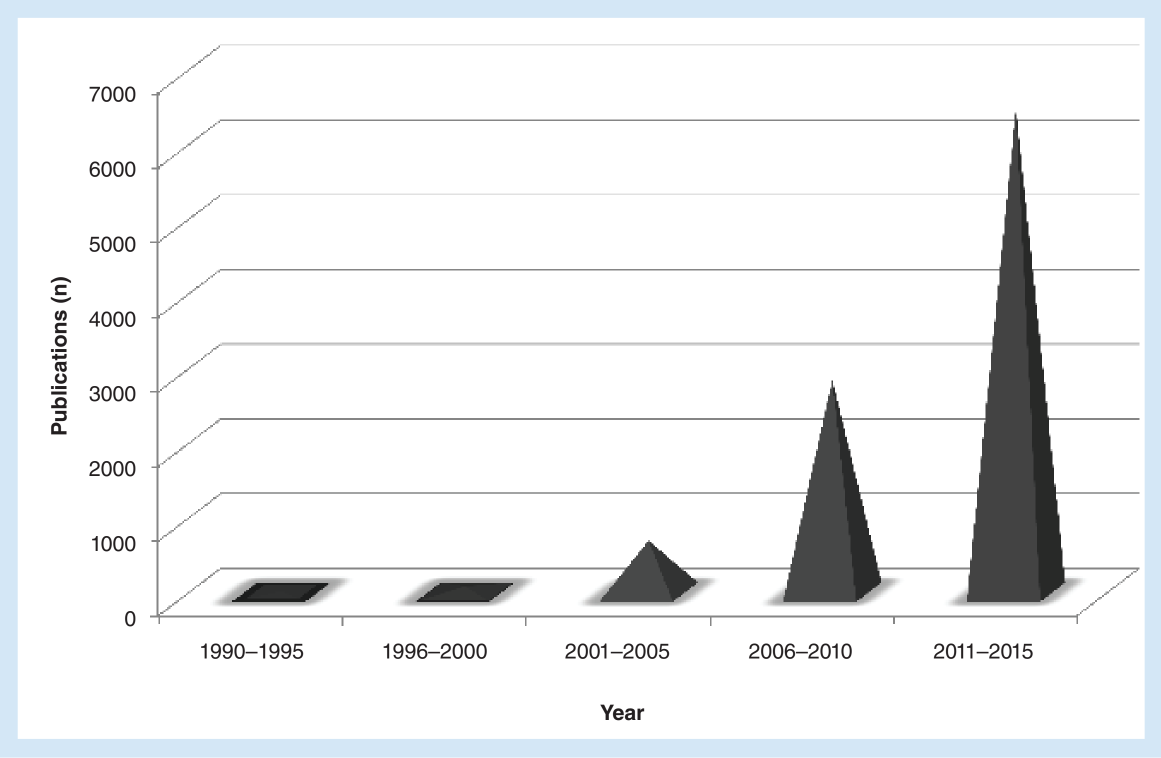

Figure 1. Exponential increase in the number of peer-reviewed publications in the field of nanomedicine. Source: PubMed; Term searched: 'nano' in title only.

tained and localized delivery of therapeutics and bioactive molecules, and have found several applications in biomedicine, including cancer [8–10], Alzheimer's [11], Parkinson's [12] and HIV [13]. Significant strides have also been achieved in imaging space with nano-particles [14–16]. Unfortunately, limitations have also been reported as it would have been expected with any new technology. For example, the clinical potential of imprinted substrates has been questioned in light of recent preclinical evidence [17,18], while nano-toxicity has raised concerns with respect to the safety of such materials [19–21].

In this special issue, we discuss various advancements in nano-fabrication technologies (e.g., two-photon polymerization [22], imprinting and electrospinning [23]) and nano-materials (e.g., liposomes [24], nanoscale bioactive glass [25], magnetically actuated biomaterials [26], nanoparticles [27–31] and electrospun fibers [32,33]) and their influence in regenerative medicine applications, such as cell programming [34], cell fate [35] and drug delivery [36]. Nanomedicine may not have completely revolutionized healthcare as yet, but it is on the way.

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